Formal Matters

It is the Examiner's position that part of the claimed inventive concept relies on the use of a Deposit and has requested a copy of the contract and that all of the necessary averments be made. In order to facilitate prosecution, Applicants submit herewith a Statement Concerning the Deposited cDNA clone assuring that the deposit has been made at the ATCC and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

The Examiner has also requested that Applicants provide an alignment showing the homology of the sequences in related applications that have been brought to the Examiner's attention. Although Applicants would like to facilitate prosecution by accommodating this request, Applicants believe doing so places an unnecessary and undesirable burden upon them. This is because accommodating this request would result in disclosing proprietary information in the instant application which is subject matter of other applications which have not been elected for prosecution nor patented. Providing this information to the Examiner would make available to the public, proprietary information that will be canceled from the related applications. Applicants respectfully submit that, the detailed information provided to the Examiner provides sufficient information to allow her, without any burden, to request a specific search and alignment information from the STIC. This is because Applicants provided information indicating which specific sequences in these related applications are related to the claimed sequences. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this request.

Objections and Rejections under Section 112

Rejections under Section 112, second paragraph

Claims 1, 6-10, 16(f), 20(f)-20(l), 20(n), 29-34, 37-39, 48, 49(f)-49(g) and 59-63 were rejected under 35 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is the Examiner's position that claims 1, 6-10, 16(f), 20(f)-20(k), 29-34, 38, 39, 62 and 63 are indefinite for failing to adequately describe the "percent identity." The Examiner alleges that " specification fails to set for[th] a definition for 'percent identity', and there are no disclosed methods by which the percent identity is determined nor are there specific parameters defined." Applicants respectfully traverse.

Applicants point out that the specification teaches that the percent identity can be determined by the Bestfit computer program which "uses the local homology algorithm of Smith and Waterman." (Specification at 17, lines 28-30.) The specification also recites specific parameters used in this determination. (Specification at 17, line 30 to page 18, line 5.) Thus, the specification sets forth sufficient guidance to allow the artisan to determine whether a sequence is "95% identical" to a reference sequence. However, in an effort to expedite prosecution, Applicants have canceled the claims reciting percent identity language without prejudice or disclaimer of the subject matter therein. Consequently, this ground for rejection should be withdrawn.

It is the Examiner's position that claims 1(f), 6-10, 16(f), 20(l), 20(n), 37-39, 49(g) and 59-65 are "indefinite, ambiguous and confusing" because these claims refer to the complement of a polynucleotide and the "polynucleotide defined in terms of an encoded amino

acid sequence but the complement would not be expected to satisfy this limitation. It is also the Examiner's position that the scope and/or intent of these claims are unclear. Applicants respectfully traverse.

Applicants disagree with the Examiner's reasoning. It is true that the rejected claims are directed to polynucleotides which are defined in terms of an encoded amino acid sequence. The skilled artisan would be able to readily determine whether a polynucleotide sequence encodes the specified amino acid sequence. Similarly, it is well known to the skilled artisan that DNA sequences are complementary. Thus, once the skilled artisan knows the sequence the coding strand of a DNA molecule, she would know the complementary, non-coding strand. Since the Examiner has agreed that the claims polynucleotides defined in terms of an encoded amino acid sequence are definite, it seems illogical that she would find the claims directed to the complement of those polynucleotides indefinite. Thus, Applicants respectfully request that the rejection be withdrawn as it is in error.

It is the Examiner's position that claim 48 is indefinite and confusing in the recitation of "any subfragment thereof" because it is not clear if the subfragment is to define the claimed fragment i.e., "said fragment is at least 100 contiguous nucleotides" or if it is intended to define the portions of the sequences enumerated in SEQ ID Nos: 5-20. Applicants respectfully traverse.

In an effort to expedite prosecution, Applicants have canceled claim 48 without prejudice or disclaimer of the subject matter therein. Thus, this ground of rejection is now moot and should be withdrawn.

It is the Examiner's position that claim 16 is indefinite in the proviso statement of "except for at lease one to fifty conservative amino acid substitutions." It is also the

Examiner's position that this proviso is indefinite because it is unclear how this defines or delineate the nucleic acids for the encoded polypeptide

In an effort to expedite prosecution, Applicants have canceled claim 16 without prejudice or disclaimer of the subject matter therein. Thus, this ground of rejection is now moot and should be withdrawn.

It is the Examiner's position that claims 20(l) and 49(f) are indefinite in the recitation that the polypeptide retains "substantially the same activity" but does not recite any specific activity for the encoded protein. It is also the Examiner's position that the use of the term "substantially" further causes the claims to be indefinite as it is a relative term. Applicants traverse.

In an effort to expedite prosecution, Applicants have canceled claims 20(l) and 49(f) without prejudice or disclaimer of the subject matter therein. Thus, this ground of rejection is now moot and should be withdrawn.

Rejections under Section 112, first paragraph

The claims [1] were rejected under 35 under 35 U.S.C. 112, first paragraph, because the specification is allegedly non enabled for 1) all nucleotide sequences defined by a specific percent identity; 2) any one to fifty conservative substitutions and any substitutions, deletions and/or additions; 3) the various epitopic regions; and 4) the various nucleotide fragments.

1) It is the Examiner's position that "the specification has not provided [an] adequate written description for sequences that are defined with percent identity, the specification has

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[1] It is not clear from the Paper No. 10 at page 4, whether the Examiner intended to reject all of the claims or only certain claims. Applicants have assumed that the Examiner rejected all of the claims.

also failed to enable all such sequences, as well as the various fragment or portions of the nucleotide sequence." (Paper No. 10 at 4-5). Applicants traverse.

In an effort to expedite prosecution, Applicants have deleted the recitations of "percent identity" from the pending claims without prejudice or disclaimer of the subject matter therein. Thus, this ground for rejection should be withdrawn.

2) It is the Examiner's position that the "specification is non-enabling for the various epitopes of the claims" because there are no examples or assurances that these regions are antigenic in nature. The Examiner concludes that the skilled artisan would be faced with undue experimentation for practicing the invention." (Paper No. 10 at 5). Applicants traverse.

The Examiner has failed to meet her burden in providing references and/or scientific analysis to support her allegation of non-enablement of the claimed invention. To establish a *prima facie* case of non-enablement, the Examiner is required to focus on the claimed invention and to provide references and/or analysis to raise a reasonable doubt that the regions specified on pages 30-33 and in Figure 3 are antigenic regions as taught by the specification. As acknowledged by the Examiner, the specification teaches which regions of the claimed protein are antigenic. This determination was made by the "Antigenic Index - Jameson-Wolf" graph shown in Figure 3 (boxed graph). The figure shows the amino acid sequence of the IL-1R AcM protein with the underlined amino acids being those that border each peak in the antigenic plot. Thus, Applicants have scientifically determined the regions of the protein appear to be antigenic.

However, in her rejection, the Examiner has merely stated that "there are not examples or assurances that these regions are antigenic in nature." She has not provided any

scientific rationale which would raise doubt that the specified regions are antigenic. It is axiomatic that the disclosure in the specification

> *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). From this it follows that the Examiner has the burden of challenging the presumptively *correct* assertions in the specification concerning how to make or use the disclosed antigenic regions of the claimed IL-1R AcM polypeptide. *Id.* at 224, 169 USPQ at 370. Only after the Examiner provides evidence showing that one of ordinary skill in the art would reasonably doubt that the specified regions of the polypeptide were antigenic nor could they be determined without undue experimentation does the burden shift to Applicants. *See In re Bundy*, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981). The Examiner has not met this initial burden.

However, in an effort to expedite prosecution, Applicants have canceled the claims directed to nucleotides encoding epitopes of the IL-1 AcM polypeptide. Thus, this ground for rejection should be withdrawn.

3) It is the Examiner's position that "the specification is non-enabling for 50 conservative substitutions and the myriad of variant that would be the result of substitution, deletion an[d]/or additions." (Paper No. 10 at 5). The Examiner alleges that "there are no structure/ function studies that would lead the skilled artisan to the regions of specific amino acid residues that can be changed/modified or deleted, with assurance that these

polynucleotides encoded for proteins that still possess the desired activity." (Paper No. 10 at 5-6). Applicants traverse.

At the outset, Applicants would like to point out that claim 16 does not require the polynucleotide encode a functional IL-1R AcM protein. The specification, at page 1, lines 14-21, teaches that such polynucleotides are useful, *inter alia*, for the isolation of the IL-1R AcM gene or allelic variants in a cDNA library, *in situ* hybridization and in Northern Blot analysis, regardless of whether or not they encode polypeptides which function as an interleukin-1R accessory molecule. A single utility is all that is required to satisfy 35 U.S.C. § 112. *See Raytheon Co. v. Roper Corp.*, 220 USPQ 592 (1983).

However, in an effort to expedite prosecution, Applicants have canceled claim16. Thus, this ground for rejection should be withdrawn.

Accordingly, the rejection of the claims under 35 U.S.C. 112, first paragraph, should be withdrawn.

Rejections under 102(a)

Claims 1, 6-10, 16 and 20-65 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Chizzonite *et al.* and Greenfeder *et al.* It is the Examiner's position that "[e]ach of the prior art discloses nucleic acid sequences for an protein that appears to [be] 100% identical to that of the claims." Applicants traverse.

Chizzonite *et al.* identifies and biochemically characterizes two classes of high-affinity IL-1 *receptors* as two different gene products, each of which are expressed in different classes of cells. This reference does not teach an IL-1 receptor accessory molecule much less the IL-

1R AcM of the present invention. Moreover, Chizzonite *et al.* does not disclose any nucleic acid or amino acid sequence information for any gene or protein. In particular, Chizzonite *et al.* does not disclose the claimed IL-1R AcM nucleic acid or amino acid sequences. Thus, reference does not provide any guidance to one skilled in the art on how to obtain the IL-1R AcM polynucleotides recited in the pending claims. It is a distinct polypeptide from the IL-1 receptor disclosed by the reference. However, there are no teachings of any kind in Chizzonite *et al.* to even suggest the existence of an IL-1R accessory molecule. Consequently, Chizzonite *et al.* do not anticipate or render obvious the claimed invention.

Greenfeder, *et al.* disclose the cloning and characterization of the *murine* IL-1 receptor accessory protein. Greenfeder, *et al.* do not teach the presently claimed human IL-1R AcM. Contrary to the Examiner's allegation, Greenfeder, *et al.* do not disclose "nucleic acid sequences for a protein that appears to be 100% identical to that of the claims." The Examiner's attention is drawn to the present specification at page 8, line 30 to page 9, line 1 and Figure 2A wherein Applicants teach that the mouse interleukin accessory protein disclosed by Greenfeder, *et al.* is only 85% identical to the protein encoded by the claimed polynucleotides. Thus, Greenfeder, *et al.* do not anticipate the claimed human IL-1R AcM polynucleotides.

Further, Greenfeder, *et al.* provide no guidance to one skilled in the art to modify the mouse polynucleotides encoding the mouse accessory protein described therein to obtain the human IL-1R AcM polynucleotides recited in the pending claims. For example, the Greenfeder, *et al.* provide no nucleic acid or amino acid sequence information for the human IL-1R AcM. In the absence of such guidance in the reference, it would constitute undue

experimentation for one of ordinary skill in the art to obtain the human IL-1R AcM polynucleotides as recited in the pending claims.

Thus, Chizzonite *et al.* and Greenfeder, *et al.*, either alone or in combination do not render the claimed invention obvious as they do not teach or suggest the claimed IL-1R AcM polynucleotides. Applicants respectfully request that the rejection be withdrawn.

Claims 20, 35, 36, 38-49, 58 and 62-65 were rejected under 35 U.S.C. § 102(a) or (b) as allegedly being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over the EST Nos H80590, T70863 or T85856. It is the Examiner's position that the disclosed sequences "are identical to a substantial portion of the nucleotide sequences of the claims" and therefore "render obvious claims which define nucleotides in terms of hybridization and the various fragments." Applicants traverse. In an effort to expedite prosecution, Applicants have canceled claims directed nucleotides encoding fragments of IL-1R AcM and nucleotides defined in terms of hybridization without prejudice or disclaimer of the subject matter therein. Thus, the rejection should be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the

Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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